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| EXAMINER | |
|---|---|
| UNGAR, SUSAN NMN | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | |

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/895,814 | XU ET AL. | |
| | Examiner | Art Unit | |
| | Susan Ungar | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on *12 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☐ Claim(s) *12,13 and 17-19* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *12,13,18 and 19* is/are rejected.

7)☐ Claim(s) *19* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/20/02,12/31/01,*10/15/01 Please note, A through 5 Addn'l Pages of IDS were found in file.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____

(12/31/01) ↑ The references found in file & were not considered. See those pages where N/A found in the file.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 17 and 12/13 as they are drawn to other than T-cell.

1. The Election filed March 12, 2004 in response to the Office Action of February 12, 2004 is acknowledged and has been entered. Claims 12, 13, 17-19 are pending in the application and Claims 12, 13 as they are drawn to immune responses other than T cell immune response and claim 17 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions. Claims 12, 13 as they are drawn to T cell responses, claims 18-19 are currently under prosecution.

2. The response to the restriction requirement of February 12, 2004 has been received. Applicant has elected Group VC, claims 18-19 for examination with traverse. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a). It is noted however, that upon review and reconsideration Examiner finds that claim 18 is in fact a linking claim and links the inventions of claims 12 and 13 only as they are drawn to a method of stimulating a T cell immune response/treating cancer in patient comprising administering to said patient at least an immunogenic fragment of the polypeptide of SEQ ID NO:525 for the stimulation of a T cell response in a human patient wherein a T cell response is stimulated/the T cell response treats the cancer.

***Specification***

3. The specification on page 1 should be amended to reflect the status of the parent applications.

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.8821 (a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reasons. First, many of the sequences in the

specification are not identified by a unique sequence identifier such as the sequences in Figures 8-9 and 11. Applicant is reminded that it is required that each sequence disclosed in the specification have a unique SEQ ID NO and that when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier must be used, either in the drawing or in the Brief Description of the Drawings. If these sequences are portions of a larger sequence which has a sequence identifier, the exact locations of these portions in the larger sequence must be provided in lieu of providing new identifiers for the portions. Applicants are given the same response time regarding this failure to comply as that set forth to respond to this office action.

Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821 (g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a).

***Priority***

5. The instant application is a CIP of several previous applications. It is brought to Applicant's attention that for the purpose of examination, priority has not been granted to the claimed prior applications whose filing dates are earlier than the filing date of Application No. 09/593,793, filed August 29, 2000 because neither the elected sequence, SEQ ID NO:525, nor the fragments of SEQ NO:525 recited in claim 19 are disclosed in Application 09/570,737 of which Application 09/593,793 is a CIP. Since among the prior applications, each is a CIP of the immediate earlier application, the prior chain thus breaks and ends with 09/593,793. Prior art published after the claimed prior applications, from which

priority is denied, but before the actual filing date of the instant application may be cited in this Office Action. If Applicant disagrees with any rejection based on Examiner's establishment of a priority date of August 29, 2000 for the instant invention, applicant is invited to submit evidence pointing to the serial number, page and line where support can be found establishing an earlier priority date.

***Claim Rejections - 35 USC 112***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 12,13,18 and 19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for stimulating and/or expanding T cells specific for the polypeptide consisting of SEQ ID NO:525 *in vitro* comprising contacting T cells with a polypeptide consisting of SEQ ID NO:525, does not reasonably provide enablement for a method for stimulating and/or expanding T cells specific for a prostate tumor protein comprising contacting T cells with at least an immunogenic fragment of the polypeptide of SEQ ID NO:525, wherein said fragment contains an amino acid sequence capable of stimulating a human T-cell response, wherein said immunogenic fragment that contains an amino acid sequence capable of stimulating a human T-cell response is selected from the group recited in Claim 19 wherein said method reads on *in vivo* use of the method or a method for stimulating a T cell response in a patient, or a method for the treatment of a cancer

in a patient. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to a method for stimulating and/or expanding T cells specific for a prostate tumor protein comprising contacting T cells with at least an immunogenic fragment of the polypeptide of SEQ ID NO:525, wherein said fragment contains an amino acid sequence capable of stimulating a human T-cell response, wherein said immunogenic fragment that contains an amino acid sequence capable of stimulating a human T-cell response is selected from the group recited in Claim 19, a method for stimulating a T cell response in a patient, and a method for the treatment of a cancer in a patient. This means not only *in vitro* stimulation and/or expanding but also *in vivo* stimulation and/or expanding. The *in vivo* stimulation and/or expanding also reads, and claims, active immunotherapy for the treatment of prostate cancer/cancer. Since the claims are also drawn to T-cell expansion *in vivo*, in a patient in the absence of limitations drawn to disease, the claims read also on the prevention of disease/prostate cancer/cancer.

The specification teaches that the present invention fulfills the need for effective means to treat prostate cancer (p. 3, lines 1-4) and teaches pharmaceutical compositions, vaccine compositions, for therapeutic applications which comprise an immunogenic polypeptide (para bridging pages 5-6) and provides methods for stimulating an immune response in a patient, preferably a T cell response in a human patient. Said method comprising administering said pharmaceutical composition wherein the methods provide treatment for the disease (p. 6, lines 23-30). The methods further provide stimulating and/or expanding T cells specific for

a polypeptide of the present invention comprising contacting T cells with SEQ ID NO:525 (page 7, lines 14-18 and p. 4, line 27). The specification teaches that the polypeptide is immunogenic, capable of eliciting an immune response, particularly a cellular immune response (p. 5, lines 8-12). The specification teaches that SEQ ID NO:525 is the amino acid sequence of P703P, encoded by SEQ ID NO:524 (p. 28). An immunogenic portion is defined as a fragment of an immunogenic polypeptide of the invention that itself is immunologically reactive with T-cell surface antigen receptors that recognize the polypeptide (p. 39, lines 16-19). MRNA expression levels of P20, a portion of the P703P gene, were found to be highly expressed in normal prostate and prostate tumor samples compared to 12 other tissues tested. There was found to be a modest increase in expression of P20 (the P703P fragment) in breast tumor, colon tumor and lung tumor when compared with normal control tissues except lung (p. 134, lines 10-15). Thus it appears, as is the case for normal prostate and tumor, that the mRNA expression in lung tumor and normal are the same. It is noted that three splice variants comprising P20, which is a 234 polynucleotide sequence encoding 78 amino acids (see SEQ ID NO:45), have been identified (p. 133, lines 24-28) but that the specification does not indicate whether or not the modest increase in mRNA expression in breast and colon tumor compared to breast and colon normal samples is due to upregulation of P703P or to one of the disclosed splice variants. The specification exemplifies the stimulation and/or expansion of T cells *in vitro* using the p5 peptide and other fragments derived from P703P pulsed into monocytes/DCs/APCs wherein the constructs were incubated with T cells, wherein some of the stimulated CTL specifically recognized some of the stimulating fragments and/or P703P (pgs 154-158). It is noted that the experimental data presented in the specification is not

commensurate in scope with the claimed invention since the claimed invention is not drawn to methods of T-cell stimulation/and or expansion/treatment with antigen presenting cells pulsed with peptides (which Examiner notes is a non-elected invention) but rather to methods of T-cell stimulation/and or expansion/treatment with "at least an immunogenic fragment of SEQ ID NO:525" which is a method of treatment with peptides or polypeptides.

One cannot extrapolate the teaching of the specification to the scope of the claims because Applicant has not enabled the breadth of the claims in view of the teachings of the specification. Factors to be considered in determining scope and enablement are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented in the specification, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7: the predictability or unpredictability of the art, and 8: the breadth of the claims. See Ex Parte Forman, 230 USPQ 546, BPAI, 1986.

Applicant has not disclosed how to make/use the claimed at least an immunogenic fragment of SEQ ID NO:525, which is in fact an active immunotherapy vaccine, in methods to treat any disease or cancer in a therapeutic regimen in humans. There is insufficient evidence of the invention with respect to the *in vivo* operability of the claimed at least an immunogenic fragment of SEQ ID NO:525 in the treatment of any disease or cancer or in the stimulation and/or expansion of T-cells specific for SEQ ID NO:525 *in vivo*. In particular, Bellone et al, Immunology Today, 1999, 20:457-462 teach the difficulties of using peptides for cancer immunotherapy, that is, that there is usually a poor correlation between induction of specific T cells and clinical responses (p. 458, last column) and

specifically lists the disadvantages of using the peptides which include no direct evidence for a role in tumor rejection, applicability to few patients, risk of generating tumor escape mutants, risk of autoimmune reactions (p. 461, Box 1). Further, the protein may be inactivated before producing an effect, such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein (See p. 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992). In addition, the claims as written read on the induction of tumor immunity for the prevention of cancer/prostate cancer/disease. However, the specification provides no information on, no guidance for which patients should be treated with the instant vaccine in order to "prevent" the occurrence of any cancer or disease, or when to start the regimen. Further, the goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease. However, Ezzell (J. NIH Res, 1995, 7:46-49) reviews the current thinking in cancer vaccines and states that tumor immunologists are reluctant to place bets on which cancer vaccine approach will prove effective in the long run (see the entire document, particularly last paragraph) and further states that no one is very optimistic that a single peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of micrometastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (p 48, para 6). In addition, Spitler (Cancer Biotherapy, 1995, 10:1-3) recognizes the lack of predictability of the nature of the art when she states that "Ask practicing oncologists what they think about cancer vaccines and you're likely to get the following response: "cancer vaccines don't work". Ask a venture capitalist or the

director of product development at a large pharmaceutical company and you're likely to get the same response." (p 1, para 1).

Furthermore, Boon (Adv Can Res, 1992, 58:177-210) teaches that for active immunization in human patients we have to stimulate immune defenses of organisms that have often carried a large tumor burden. Establishment of immune tolerance may therefore have occurred and it may prevent immunization and several lines of evidence suggest that large tumor burdens can tolerize or at least depress the capability to respond against the tumor (p. 206, para 2). Given the above it is not clear why, if SEQ ID NO:525 is expressed *in vivo*, Applicant would expect that an immune response could be generated against the self antigen. There is no suggestion in the specification that the expression of these antigens has resulted in autoantibodies or CTX against the antigen thus it would be highly unpredictable that administration of the antigen, as a cancer vaccine, into patients that already express a heavy load of the antigen would lead to an immune response against any tumor.

Even if T-cells could be induced, Sherman et al, (1998, Critical reviews in Immunol, 18(1-2): 47-54) teach that self-tolerance may eliminate T cells that are capable of recognizing antigen epitopes with high avidity . In other words, only CTLs with low affinity are left, which would not be effective for tumor treatment *in vivo*. Smith (1994, (Clin Immunol, 41(4): 841-849), teaches that antigen overload, due to antigen shedding by actively growing tumor, could block specifically either cytotoxic or proliferative responses of tumor specific T cells (p. 847, last paragraph bridging p.848 and p.848). Smith further teaches that many tumors progressively lose MHC representation at the surface of the cell, and the loss of surface Class I MHC could severely limit the possibilities for cytotoxic T

cells specific for a tumor specific antigen to find said tumor specific antigen in the necessary MHC context (p.484). In agreement, Boon, *Supra* teaches even if activated CTLs are significantly increased, the therapeutic success remains unpredictable due to inconsistencies in antigen expression or presentation by tumor cells (p.178, paragraph before last paragraph).

Furthermore, as drawn specifically to prostate cancer immunization, Hodge et al (Int. J. Cancer, 63:231-237, 1995) specifically discloses that previous attempts to actively immunize patients with prostate adenocarcinoma cells admixed with adjuvant showed little or no therapeutic benefit (p. 231, col 1, first paragraph of Introduction). The prostate adenocarcinoma cells and normal prostate cells express common antigens. Given that the specification teaches that the polynucleotide that would encode SEQ ID NO:525 is equally expressed in normal and malignant prostate tissue, if the polypeptide of SEQ ID NO:525 is in fact expressed *in vivo*, it would be expected that it would be expressed both in the normal cells and the tumor cells and that fragments of SEQ ID NO:525 would be found on MHC molecules on the surface of the cells. Given this clear demonstration of the lack of efficacy of the attempt to actively immunize patients with prostate adenocarcinoma cells which would be expected to present the claimed "at least immunogenic fragments" to the immune system, no one of skill in the art would believe it more likely than not that at least an immunogenic fragment of SEQ ID NO:525 would effectively actively immunize patients with prostate cancer or any other type of cancer.

In particular, as drawn to immunogenic fragments in clinical trials for T-cell therapy for prostate cancer, Murphy et al (The Prostate, 1996, 29:371-380) specifically teach a phase I clinical trial for T-cell therapy for prostate cancer using

autologous dendritic cells pulsed with HLA-specific peptides from PSMA antigen. The reference teaches that two components are required for the production of an effective T-cell immune response. The first component is that of cancer-specific antigens and the second is the requirement of efficient presentation of cancer antigen by the host's antigen presenting cells to circulating T cells in the generation of an effective anticancer response (see pages 171-172). The treatment group participants were divided into five treatment groups. The first group received the PSM-P1 peptide, the second group received the PSM-P2 peptide, the third group received autologous DC, and groups 4 and 5 received DC pulsed with either PSM-P1 or PSM-P2 (p.373, col 2, see Treatment Groups). Data from immunological monitoring studies show an increase of T cell response in Groups 4 and 5 but no significant response in Groups 1-3. These results demonstrate the requirement to have both components in the generation of an effective immune response (p. 379, para bridging cols 1 and 2). The results clearly demonstrate that the administration of prostate peptides, in the absence of pulsing into APC, did not result in effective stimulation and/or expansion of T-cells.

As drawn to the "at least immunogenic fragments" for the stimulation and/or expanding of T-cells specific for SEQ ID NO:525, the specification teaches that the fragments consisting of the range of amino acids recited in Claim 19 were effecting in stimulating and/or expanding T cells specific for SEQ ID NO:525 *in vitro*, when pulsed into antigen presenting cells and also clearly teaches that numerous other sequences that were predicted to be T-Cell epitopes did not in fact produce an appropriate T-cell response wherein the T-cell lines produced using the peptide/APC construct were either peptide specific only or were non-responsive to any antigen tested (p. 158, lines 1-4). In corroboration of the teaching in the

specification of the unpredictability of epitope prediction, Lamb et al (The EMBO J., 1987, 6:1245) specifically teaches that of six peptides that were predicted to be T cell determinants, only two were shown to contain human T cell epitopes (see abstract). Given the above, it is clear that although predictions can be made as to T-cell epitopes, it is also clear that each of those predictions must be individually tested, essentially leaving the practitioner to determine effective T-cell epitope peptides by random experimentation, which is undue.

As drawn to the T-cell specific immunogenicity of peptides, Berzofsky, (ASM News, 2004, 70:219-223) specifically teaches that among the factors critical in developing T cell-based vaccines, the most stringent appears to be the affinity of the peptide for the MHC molecule. All else being equal, higher-affinity peptides are generally more immunogenic and peptides with very low affinity for MHC molecules are rarely immunogenic. Therefore, selecting high-affinity peptides and modifying peptides to increase their affinity for MHC may be critical factors for developing effective vaccines (p. 220, col 1). Although the specification reported that T-cell line1-F9 was very sensitive to the p5 P703P peptide and therefore likely to have a high affinity for the epitope (pgs 154-158), the specification provides no information on the affinity of the claimed moieties (containing "at least immunogenic fragments of SEQ ID NO:525") for the MHC molecule or whether or not, *in vivo*, any fragments of SEQ ID NO:525 have sufficient affinity for the MHC molecule to lead to the production of sufficient T-cells to function as claimed and contemplated.

The critical nature of immunogenicity of the peptides for induction of T-cell immunity/response is further exemplified by the following. Kirkin et al (1998, APMIS, 106 : 665-679) review several melanoma-associated antigens, including

NY-ESO1, and conclude that initiation of a strong immune response *in vivo* is an extremely rare event (p.674, first column, last paragraph). Kirkin et al teach that for some antigens, due to the existence of self-tolerance, only T cells with low affinity T-cell receptors are produced (abstract). Kirkin et al teach that although several peptides of melanoma associated antigens have been identified as recognized by CTL *in vitro*, and peptides from MAGE-A1 and MAGE-A3 have been tested for their ability to induce anti-melanoma immune response *in vivo*, only one of the peptides, peptide EVDPIGHLY of MAGE-A3, has limited anti-tumor activity, indicating their low immunogenicity (p.666, second column, second paragraph, last 6 lines). Further, even this peptide EVDPIGHLY of MAGE-A3 produces a very low level of CTL response which is detectable only by a very sensitive method, as taught by Chaux et al, (Int J Cancer, 1998, 77: 538-542, abstract). In addition, even if the data presented in the specification were to be compensate in scope with the claimed invention, the *in vitro* demonstrations of CTLs stimulation/expansion by the fragment/APC constructs could not be extrapolated to the invention as claimed and contemplated, because the CTLs are continuously in contact with targets in *in vitro* assays and are not subjected to the defense of the body. This is demonstrated by Chaux et al, *Supra*, who further teach some of the CTLs have an affinity that is too low for the recognition of cells that have processed the antigen, which is different from the *in vitro* conditions in which the synthetic peptides are in high number when incubated with the cells (p.541, second column, second paragraph).

Thus based on the teaching in the art and in the specification, one cannot predict that an adequate *in vivo* T cell response useful for immunotherapy, as

contemplated and claimed, could be induced by the claimed "at least immunogenic fragment of SEQ ID NO:525" in patients having tumor burden.

Finally, it is well known that the art of anticancer drug discovery for cancer therapy is highly unpredictable, for example, Gura (Science, 1997, 278:1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile and teach that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see first and second para). Because of the known unpredictability of the art, in the absence of *in vivo* evidence, no one skilled in the art would accept the assertion that the invention would function as contemplated and as claimed. Further, the refractory nature of cancer to drugs is well known in the art. Jain (Sci. Am., 1994, 271:58-65) teaches that tumors resist penetration by drugs (p.58, col 1) and that scientists need to put expanded effort into uncovering the reasons why therapeutic agents that show encouraging promise in the laboratory often turn out to be ineffective in the treatment of common solid tumors (p. 65, col 3). Curti (Crit. Rev. in Oncology/Hematology, 1993, 14:29-39) teaches that solid tumors resist destruction by chemotherapy agents and that although strategies to overcome defense mechanisms of neoplastic cells have been developed and tested in a number of patients, success has been limited and further teaches that it is certainly possible that cancer cells possess many as yet undefined additional molecular mechanisms to defeat chemotherapy treatment strategies and if this is true, designing effective chemotherapeutic regimens for solid tumors may prove a daunting task (para bridging pages 29-30) and concludes that knowledge about the physical barriers to drug delivery in tumors is a work in progress (p. 36,

col 2). The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the invention would function as claimed and given the information in the art, no one of skill in the art would believe it more likely than not that the invention would function as claimed or contemplated in the *in vivo* environment with a reasonable expectation of success. In view of the above, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

***Double Patenting***

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 12 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7 of U.S. Patent No. 6,613,872. Although the conflicting claims are not identical, they are not patentably distinct from each other because they relate to the same inventive concept, that is a method for stimulating an immune response with at least an immunogenic fragment of SEQ ID NO:525 which is capable of eliciting a human T-cell response. The patented claim is drawn to a method for stimulating an immune response in a patient, comprising administering a composition comprising SEQ ID NO:172 which is at least an immunogenic fragment of the polypeptide of SEQ ID NO:525 in that SEQ ID NO:172 is 100% identical to SEQ ID NO 525 residues 1-159, especially in view of the teaching in the specification that an "immunogenic portion used herein is a portion of an antigen that is recognized by B-cell and/or T-cell surface antigen receptors (see paragraph 24 of Detailed Description text attached hereto). It would be expected that a fragment consisting of 63% of SEQ ID NO:525 would contain T cell epitopes. It is noted that SEQ ID NO:172 comprises the sequences claimed in claim 19 wherein the sequences include amino acid residues 110-124, 125-139, 135-149 of SEQ ID NO: 525.

**Claim Objections**

9. Claim 19 is objected to as being dependent upon a non-elected claim. Appropriate correction is required.

10. No claims allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at (571) 308-3995. The fax phone number for this Art Unit is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1640.

Susan Ungar
Primary Patent Examiner
May 14, 2004